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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/734,696	12/13/2000	Ernesto Freire	03940022BA	6797

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EXAMINER

MORAN, MARJORIE A

ART UNIT PAPER NUMBER

1631

DATE MAILED: 11/07/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/734,696

Applicant(s)

FREIRE ET AL.

Examiner

Marjorie A. Moran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 July 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-4,6-10,13,15 and 17 is/are pending in the application.
- 4a) Of the above claim(s) 3,4,15 and 17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,6-10 and 13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Election/Restrictions

Applicant's election without traverse of Group I, claims 2, 6-10 and 13, in Paper No. 6, filed 7/31/02, is acknowledged.

Claims 3-4, 15 and 17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 6.

Priority

If applicant desires priority under 35 U.S.C. 119 (e) based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. For example, the phrase --and claims benefit to Provisional US Application 60/066,495, filed 11/24/1997-- should be added to the end of the priority statement added in the amendment filed 12/13/00.

The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within

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this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions, Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

The instant declaration claims priority to two Provisional Applications, but support for the instant claims is found in only one. Provisional Application 60/048,274 discloses a Figure 1 which shows most of the claimed method steps. However, the provisional's Figure 1 does not disclose a step of determining the three-dimensional coordinates of an energy minimized structure of a selected compound when that compound is bound to a binding site. 60/048,274 discloses various methods for designing an ideal ligand and predicting binding affinities, but other than in the Figures, does not disclose actual method steps for predicting a binding affinity. 60/048,274 does not disclose a method comprising a step of determining the three-dimensional coordinates of an energy minimized structure of a selected compound when that compound is bound to a binding site anywhere. Provisional application 60/066,495, filed 11/24/1997, provides support for the instantly claimed methods, specifically on page 13. For these reasons, priority is not granted to the filing date of 60/048,274. Priority for the instant claims is granted only to the filing date of Provisional Application 60/066,495, of 11/24/1997.

Information Disclosure Statement

The information disclosure statement filed 12/13/2000 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but all of the information referred to therein has not been considered.

Reference AG on page 1 is duplicative of reference AC on the same page (US 5,642,292), therefore reference AG has been crossed out and reference AC initialed to indicate consideration. References FH, FI, and FJ were not found in either the instant application or with parent application 09/089,097. As these references were not supplied with the IDS in either the instant or parent application, they have not been considered, and are crossed out to indicate nonconsideration.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Specification

The abstract of the disclosure is objected to because the first "sentence" is not complete. Appropriate correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 6, 8, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by DELISI et al. (US 5,495,423).

DELISI teaches a computer assisted method and program for predicting the binding affinity of a ligand to a selected binding site wherein the coordinates and identity of atoms from a receptor molecule are input into a computer, as is information for atoms of a selected ligand (amino acid or acids), a model of two generated, energy of the complex (3D model) minimized, and a binding affinity of the compound for its binding site predicted from the energy minimized structure (col. 5, line 55-col. 6, line 26 and col. 7, line 55-col. 8, line 9), thereby anticipating claim 13. As DELISI's input, output, and processing of data necessarily require the computer performing those functions to have an input device, output device, and a processor, therefore claim 2 is anticipated. AS DELISI teaches that his method may be performed with peptides comprising two or more amino acids (col. 6, lines 13-15), and specifically with dipeptides (col. 13, Example 2) or larger peptides (Examples 3 and 4), claims 6 and 8 are also anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject

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matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 6-10 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of DELISI et al. (US 5,495,423) and SHAKHNOVICH et al. (US 5,854,992, filed 9/26/1996).

The claims recite methods of predicting the binding site of a ligand, specifically a peptide, for a binding site of a selected molecule wherein data including the identity and three-dimensional (3D) coordinates of the atoms in the binding site of the selected molecule are entered into a computer, the identity and 3D coordinates of a ligand are entered, a model of the ligand bound to the binding site is generated, the coordinates of an energy minimized structure of the ligand when bound are determined, and the binding affinity determined based on the energy minimized structure. Claim 6 limits the ligand to a dipeptide. Claim 7 limits the method of claim 6 to a repetition of the method steps for a plurality of dipeptides, and recites a step of identifying the dipeptide with highest determined binding affinity as a lead peptide. Claim 8 limits the method of claim 2 to further comprise steps of selecting a first polypeptide of 3 or more amino acids, and predicting the binding affinity of the selected peptide. Claim 9 limits the method of claim 8 to selection of a second polypeptide (longer) comprising the first polypeptide,

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and determining the binding affinity of the second polypeptide. Claim 10 limits the method of claim 8 to one wherein a variant of the first polypeptide is selected and a binding affinity of the variant is determined. Claim 13 recites a computer program, residing on a computer readable medium, for performing the method.

DELISI teaches a computer assisted method and program for predicting the binding affinity of a ligand to a selected binding site, as set forth above. DELISI does not teach comparison of dipeptides nor an iterative process nor use of variants of peptides.

SHAKHNOVICH teaches that methods of docking (determination of binding parameters) are known wherein amino acids are added to a peptide and the energy minimized in an iterative process (col. 4, lines 52-62). SHAKHNOVICH also teaches keeping the "best 10-100 low energy structures", thus suggesting comparison of variant peptides.

It would have been obvious to one of ordinary skill in the art at the time of invention to have incorporated the concept of "growing" a larger peptide from a smaller one, as taught by SHAKHNOVICH, into the method of DELISI where the motivation would have been to design peptides complementary to proteins of a known structure (i.e. to the binding site of DELISI), as taught by SHAKHNOVICH (col. 4, lines 52-54). It would further have been obvious to have compared either the dipeptides of DELISI, or variant larger peptides, to any other peptide in the method of DELISI in order to pick a "lead peptide", as suggested by the teaching of SHAKHNOVICH for keeping the lowest energy structures, where the motivation would have been to find and keep the structure/peptide with the most favorable (i.e. lowest free energy) interaction, as taught by both DELISI (col. 5, lines 23-50) and SHAKHNOVICH (col. 1, lines 53-65).

Conclusion

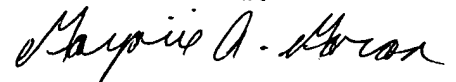
Claims 2, 6-10 and 13 are rejected; claims 3-4, 15 and 17 are withdrawn. The specification is objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the LIE, Tina Plunkett, whose telephone number is (703) 305-3524.

MARJORIE MORAN
PATENT EXAMINER



November 4, 2002